William R. Fairweather, PhD, PSTAT®

Flower Valley Consulting, Inc.
3310 N. Leisure World Blvd, Unit 931
Silver Spring MD 20906

1998 to Present

President and Principal in this statistical consulting firm. Responsible for all executive and managerial decisions as well as technical matters. Areas of activity include clinical and preclinical study design and data analysis, methodological research in statistics, and computer program validation. Expert regulatory statistician (FDA designation). Areas of application include clinical trial design and analysis, missing data analyses, interim analyses, pharmacokinetics, bioavailability and bioequivalence, chemistry and manufacturing controls, stability studies (including bracketing and matrixing), animal safety studies, and carcinogenicity studies. Service on Data Safety Monitoring Committees. Litigation support and expert witness. Clients include the largest and the smallest (virtual) US biopharmaceutical firms.

Center for Drug Evaluation and Research (CDER)
Food and Drug Administration (FDA)
Rockville MD 20857

1996 to 1998
Associate Director, Office of Epidemiology & Biostatistics

Responsible for drafting policy, interpreting regulations, developing standards. Member of the OEB management team. Also serving as Executive Director for Information Technology for OEB. Principal advisor to the Office, including the Director and Deputy Director, on matters pertaining to research, development, and application of information technology, scientific computing and statistical methods in evaluation of drug chemistry and drug product quality, animal toxicology, drug safety, and clinical trial data quality assurance. Provide scientific leadership. Conduct and coordinate research in statistical methodology, provide expert consultation. Principal, authoritative spokesperson for OEB in these areas of responsibility.

1979 to 1996
Chief, Statistical Application & Research Branch

Provide statistical support to all areas of the Center for Drug Evaluation & Research and (until 1990) the Center for Biologics Evaluation & Research; ie, clinical trial evaluation for safety and efficacy of AIDS and other anti-viral drugs, biologicals, animal tumorigenicity testing, bioequivalence, epidemiology, and compendial standards. Responsible for directing the statistical program, for planning and allocating resources, and for the quantity and quality of work produced by three subordinate units of the Branch (18 professionals, l secretary). Participate in setting of short- and long-range goals for the Division of Biometrics.

1990
Acting Director, Division of Biometrics

Temporary promotion (6 months) while supervisor was overseas. Supervised 2 Branch Chiefs and a Division of over 50 professionals.

1976 to 1979
Group Leader, Statistical Evaluation Branch

First line supervisor of 5 Ph.D. level statisticians and a secretary. Responsible for the quantity and quality of work produced by the Group, which includes approximately 100 technical reports covering clinical trial evaluations for half the prescription drugs approved each year in the U.S.

1973 to 1976
Mathematical Statistician

Perform critical scientific reviews and evaluations of data and statistical methodology submitted by industry in support of New Drug Applications. Develop new methods of statistical analysis, as needed. Present authoritative statistical position of FDA in meetings with medical, legal and statistical personnel from industry.

Biostatistics Department, University of Washington,
Seattle, Washington.

1971 to 1973
Statistical Consultant. Parttime while completing doctorate.

Biometrics Branch, National Heart and Lung Institute,
National Institutes of Health, Bethesda, Maryland.

1968 to 1971
Statistician (Lt., U.S. Public Health Service).

Provide consulting services to intramural laboratory researchers involving design of experiments, data analysis by desk calculator and computer, and interpretation of results.

Education

PhD, University of Washington, Biomathematics, l973
MS, Cornell University, Statistics, l966
AB, University of California, Berkeley, Mathematics and Statistics, l964

Research Interests

Multiple imputation
Interim analyses
Adaptive designs
Forensic science statistics

Honors

Accredited Professional Statistician, American Statistical Association, 2011
Harvey W. Wiley Medal and FDA Commissioner's Special Citation "for outstanding and sustained application of statistical methodology in the areas of postmarketing risk assessment, carcinogenicity, and animal toxicology with the aim of promoting public health." 1999
Group Recognition Award for service on Carcinogenicity Assessment Committee, 1997
Commissioner's Special Citation for service on Tobacco Working Group, 1994
Commendation for performance as Acting Division Director, 1991
US Public Health Service Special Recognition Award, 1987
Food and Drug Administration Commendable Service Awards, l980 and 1983
Food and Drug Administration Award of Merit, l976
Sigma Xi-RESA, l975
Listed in Who's Who in American Science
U.S. Public Health Service NIH Predoctoral Fellow, University of Washington, l970-l973
John McMullen Graduate Fellow, Cornell University, l964-5
A.B. with Honors, University of California, l964

Memberships

American Statistical Association
Biometric Society
Federal Executive Institute Alumni Association
Food & Drug Administration Alumni Association

Other

I program in R, SPlus, SAS, Access, and Excel. I have created a website using HTML and ASP. I wrote and published three R extensions, the first implementing a novel statistical test, the second providing a new tool for the study of matrix determinants, and the third provides a forward searching procedure for assessing outliers in clinical trials and laboratory studies. In addition to English, I speak French and Hebrew, I understand some Spanish and German. I am studying Japanese.

I enjoy a number of activities in addition to my professional work. Among these are martial arts and sailing. I hold a yondan (4th degree black belt) in aikido, a chuden (2nd degree black belt) in ki development, and an assistant examiner certificate. I am the Head instructor for the Maryland Ki Society and I operate a dojo in Olney/Sandy Spring Maryland. I teach aikido for the Montgomery County Department of Recreation.

I am a longtime sailor, and I own a 2003 ComPac 35 sloop. My wife and I sail her primarily in Chesapeake Bay. In the fall of 2007 and again in 2010 we travelled down the IntraCoastal Waterway to Florida and back on our boat. We lived and worked aboard in the winter and we returned to Chesapeake Bay in the spring. In the spring of 2011 we cruised her to the Bahamas. I have sailed in the Caribbean and the South Pacific

I have served as a referee for the National Academy of Sciences/National Research Council, for the journal *Statistics in Biopharmaceutical Research* and for the *Journal of Forensic Investigative Accounting*. I have contributed to a Wikipedia article.

I have mentored several junior statisticians as part of an American Statistics Association program.

Bibliography

William R. Fairweather, PhD

Statistical analysis packages in R

Fairweather, WR (2022) forsearch: Outlier Diagnostics for Some Linear Effects and Linear Mixed Effects Models. R package version 1.0.0 https://CRAN.R-project.org/package=forsearch

Fairweather, WR (2021) *SymbolicDeterminants*: Symbolic Representation of the Determinant of a pxp Matrix. R package version 2.0.0. https://CRAN.R-project.org/package=SymbolicDeterminants

Fairweather, WR (2020) *MVNtestchar*: Test for Multivariate Normal Distribution Based on a Characterization. R package version 1.0.0. https://CRAN.R-project.org/package=MVNtestchar

Fairweather, WR (2020) *SymbolicDeterminants*: Symbolic Representation of the Determinant of a pxp Matrix. R package version 1.2.0. https://CRAN.R-project.org/package=SymbolicDeterminants

Book chapter

Fairweather, WR and TY Lin (1998). Statistical and Regulatory Aspects of Drug Stability Studies. Chapter 5 of International Stability Guidelines, edited by D Mazza, Buffalo Grove IL: Interpharm Press, Inc.

Online publication

Fairweather, WR. A computer-assisted, multiple-choice approach to learning Japanese kanji. www.marylandkiaikido.org/kanjifirst.pdf

Papers

1. Fairweather, WR Evaluation of alternative approaches to preliminary testing in stability studies with missing data. In preparation

2. _____ Calculating the expiration dating period of a stability study that includes missing values. In preparation.

3. _____ The imputer's model—Different model possibilities with the same data and how to proceed. In preparation.

4. _____ Theoretical and practical aspects of the Benford distribution of leading digits. In preparation

5. Calzetta,L; Matera,MG: Goldstein,MF; Fairweather,W; Howard,WW; Cazzola,M; Rogliani,P. (2020) A Long-term clinical trial on the efficacy and safety profile of doxofylline in asthma: the LESDA study. *Pulmonary Pharmacology and Therapeutics*, **60**, 101883.

6. Fairweather, WR (2018) Detecting fraud in non-Benford transaction files. *J. Forensic Investigative Accounting,* **10**,2, 258-266. http://web.nacva.com/JFIA/Issues/JFIA-2018-No2-7.pdf

7. _____ (2017) Sensitivity and specificity in application of Benford's Law to explore for potential fraud. *J. Forensic Investigative Accounting,* **9**,3, 953-961. **https://s3.amazonaws.com/web.nacva.com/JFIA/Issues/JFIA-2017-No3-7.pdf**

8. Murugesan, SR; King, CR; Osborn, R; Fairweather, WR; O'Reilly, EM; Thornton, MO; and Wei, LL. (2009) Combination of human tumor necrosis factor-alpha gene delivery with gemcitabine is effective in models of pancreatic cancer, *Cancer Gene Therapy*, 1-7.

9. Posner, M; Chang, KJ; Stephenson, J; Khan, M; Reid, T; Fisher, W; Thornton, M; Kovacevic, M; Fairweather, W; Thompson J; Rosemurgy, (2009) A. Multi-center Phase II/III Randomized Controlled Clinical Trial using TNFerade gene delivery combined with chemoradiation in patients with locally advanced pancreatic cancer: Interim survival analysis trend favors TNFerade. *Cancer Gene Therapy* 16, 841-847| doi:10.1038/cgt.2009.32

10. Fairweather WR. (2013). Preliminary testing in multifactor stability studies. *Statist. Biopharm. Research*, **5**(4), 338-344.

11. _____ (2012). Rejoinder to Buck and Altan, *J. Biopharm. Statistics*, **22**(01), 211-212.

12. _____ (2012). Corrigenda, *J. Biopharm. Statistics*, **22**(01), 221-221.

13. _____ (2011). Ambiguous assignment of release values in stability studies. *Jnl Biopharm Statist.* **21**(03), 453-471.

14. Thompson, R; Ackerman, SJ; Watrous, RL. (2008) The impact of computer-assisted auscultation on physician referrals of asymptomatic patients with heart murmurs. (Statistical contribution by Fairweather, W). *Clin. Cardiol*. 31(2),79-83

15. Fairweather, WR (2005). An application of the Mantel-Haenszel statistic in process validation. *J. Biopharm. Statist*. 15 253-264.

16. _____ (2003). A quantitative assessment of factors influencing the probability of postmarketing out-of-specification observations. *J.Biopharm.Statist*. 13(3) 415-423.

17. _____, R Mogg, PS Bennett, J Zhong, C Morrissey, and TL Schofield (2003). Monitoring the stability of human vaccines. *J.Biopharm.Statist.* 13(3) 395-413.

18. _____ (2001). Comments on ICH Q1D. Position paper submitted to rapporteur of International Conference on Harmonisation.

19. _____, A Bhattacharyya, PP Ceuppens, G Heimann, LA Hothorn, RL Kodell, KK Lin, H Mager, BJ Middleton, W Slob, KA Soper, N Stallard, J Ventre, J Wright (1998). Biostatistical methodology in carcinogenicity studies. *Drug Information Journal*,32(2):401-421.

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21. Contrera, J, A Jacobs, J DeGeorge, CH Chen, JB Choudary AF DeFelice, WR Fairweather, et al. (1998) Carcinogenicity testing and the evaluation of regulatory requirements, *Virtual Journal of the Center for Drug Evaluation & Research*, 1.

22. Fleming, GA, WR Fairweather, JG Levine and J Woodcock. (1998) FDA review of the metformin New Drug Application, *Virtual Journal of the Center for Drug Evaluation & Research*, 1.

23. Fairweather, WR (1996). Integrated safety analysis: Statistical issues in the assessment of safety in clinical trials. *Drug Information Journal*, 30, 875-9.

24. _____, D Lin and R Kelly (1995). Regulatory, design and analysis aspects of complex stability studies. *J.Pharm.Sci*. 84 no 11., 1322-1326.

25. DeMets, DL, D Anbar, WR Fairweather, TA Louis and RT O'Neill (1995). Training the next generation of biostatisticians. *The American Statistician*, 48, 280-5.

26. Temple, R, Fairweather, WR, V Glocklin, RT O'Neill (1988). The case for blinded slide reading. *Comments Toxicology*, 2, 99-109.

27. Fairweather, WR (1987). Comparing proportion exposed in case-control studies using several control groups. *Am. J. Epid*, 126 No 2, 170-178.

28. Hurwitz, ES, MJ Barrett, WJ Gunn, D Bregman, P Pinsky, LB Schonberger, JS Drage, RA Kaslow, DB Burlington, GV Quinnan, JR LaMontagne, WR Fairweather, D Dayton, WR Dowdle (1987). Public Health Service Study of Reye Syndrome and medications--Report of the main study. *JAMA*, 257 No 14, 1905-1911.

29. Shah, VP, JP Hunt, WR Fairweather, VK Prasad, and G Knapp (1986). Influence of dioctyl sodium sulfosuccinate on the absorption of tetracycline. *Biopharmaceutics & Drug Disposition* 7, 27-33.

30. Hurwitz, ES, MJ Barrett, D Bregman, WJ Gunn, LB Schonberger, WR Fairweather, et al (1985). Public Health Service study of Reye's syndrome and medications--Report of the pilot phase. *New Eng J Med,* 313, No.14, 849-857

31. Fairweather, WR (l98l). Distribution-free comparison of multiple tumor incidence in the presence of unrelated censoring. *Amer. J. Math. Management Sci*.,l, 267-288.

32. Anello, C and WR Fairweather (l98l). Statistical principles in the regulatory process. *Pharm. Tech*., November, 90-97.

33. Shosteck, H and WR Fairweather. (l979). A comparative analysis of physician response rates to mail and personal interview surveys. *Public Opinion Quarterly* 43, 206-2l7.

34. Fairweather, WR (l977). Investigating relationships between in vivo and in vitro variables for the purpose of prediction. *J. Pharmacok. Biopharm.* 5, 405-4l8.

35. _____ (l976). Bioequivalence studies as examples of the use of crossover designs. Paper presented to the Biometric and Epidemiological Methodology Advisory Committee, Food and Drug Administration.

36. _____ (l976). Multiple comparisons and multiple testing for combination drugs. Paper presented to the Biometric and Epidemiological Methodology Advisory Committee, FDA.

37. _____ (1973). A test for multivariate normality based on a characterization. Dissertation submitted in partial fulfillment of the requirements for the Doctor of Philosophy, University of Washington, Seattle WA.

38. _____ (l972). A method of obtaining an exact confidence interval for the common mean of several normal populations. *Appl. Statist*. 2l, 229-233.

39. _____ (l972). A test for multivariate normality based on a characterization (preliminary report). *Bull. Instit. Math. Statist*. l, l37.

40. Lee, HG, AW Cheever and WR Fairweather (l97l). Influence of parasite strain on chemotherapy of murine infections with Schistosoma mansoni. *Bull. Wld. Hlth. Org.* 45, l47-l55.

41. Fairweather, WR (l968). Some extensions of Somerville's procedure for ranking means of normal populations. *Biometrika* 55, 4ll-418.

Presentations

1. Kim,AHJ, Strand,V, Mathis, NL, Fairweather, WR, et al (2015) Circulating levels of iC3b and C3 levels correlate with SLEDAI-2K Responder Index-50 (S2K RI-50) disease activity scores—the CASTLE (Complement Activation Signatures in Systemic Lupus Erythematosus (SLE)) study. Lupus Conference, Vienna Austria.

2. Kim, AHJ, Strand,V, Mathis, NL, Fairweather, WR, et al (2015) Circulating levels of iC3b, C3 and prednisone levels are predictive of SLEDAI-2K Responder Index-50 (S2K-RI50) disease activity scores—the CASTLE (Complement Activation Signatures in Systemic Lupus Erythematosus) study. EULAR Conference, Rome Italy.

3. Fairweather, WR (1998). FDA review. Panel discussion in Workshop on Assuring Data Quality and Validity in Clinical Trials for Regulatory Decision- Making. Institute of Medicine of National Academy of Sciences.

4. _____ (1996). Regulatory, design and analysis aspects of complex stability studies - A US perspective. Invited paper presented at conference on Stability Testing - Design and Interpretation of Data for International Registration of Pharmaceuticals for Human and Veterinary Use. London, Great Britain.

5. _____ (1996). Issues in carcinogenicity analyses - An FDA perspective. Invited paper presented at Drug Information Association Workshop on Statistical Methodology in Nonclinical and Toxicological Studies, Brugge Belgium.

6. _____ (1995). Integrated safety analysis: Statistical issues in the assessment of safety in clinical trials. Paper presented at 31st Annual Drug Information Association meeting. Orlando FL.

7. _____ (1994). TQM in Drug Development. Discussant for three papers at American Statistical Association Winter Meeting, Atlanta GA.

8. _____ (1994). Design of Stability Studies: FDA Statistical Perspective. Invited paper presented at American Association of Pharmaceutical Scientists Workshop on Stability Guidelines for Testing Pharmaceutical products, Arlington VA.

9. _____ (1994). Statistical analysis of stability data according to the new requirements. Invited paper presented at conference on Statistical Testing - Design & Interpretation of Data for International Registration of Pharmaceuticals, London, Great Britain. Also presented at Medicines Control Agency, Department of Health, London.

10. _____ (1994). Statistical Issues of Chemistry and Manufacturing Controls. Discussant for four papers at Joint Meetings of the American Statistical Association, Toronto Canada.

11. _____ and SD Dubey (1994). Statisticians, the FDA and a time of transition. Keynote address presented at Pharmaceutical Manufacturer's Association Education and Research Institute course in Non-Clinical Statistics, Washington DC.

12. _____, D Lin and R Kelly (1994). Regulatory and design aspects of complex stability studies. Presented at the Pharmaceutical Research and Manufacturers of America Biostatistics Subsection/Clinical Data Management Group Joint Meeting, Washington DC.

13. _____ and SD Dubey (1993). Statisticians, the FDA and a time of transition. Keynote address presented at Pharmaceutical Manufacturer's Association Education and Research Institute course in Non-Clinical Statistics, Washington DC.

14. _____ and RT O'Neill (1993). Training the next generation of biostatisticians - A view from Government. Presented at Joint Meeting of the Biometric Society, ENAR. Philadelphia PA.

15. _____ (1992). TQM at FDA. Invited paper presented at the national meeting of the American Statistical Association, Boston MA.

16. _____ and SD Dubey (1992). Statisticians, the FDA and a changing world. Keynote address presented at Pharmaceutical Manufacturer's Association Education and Research Institute course in Non-Clinical Statistics, Washington DC.

17. _____ (1991). Does "one size fits all" apply to animal carcinogenicity studies? Paper presented at Regulatory Affairs Professional Society meeting on International Toxicology Guidance: Scientific and Regulatory Aspects. Lucca, Italy.

18. _____ and DJ Schuirmann (1991). Outliers in bioequivalence studies - Should they be included? Paper presented at the Drug Information Association workshop on Bioavailability/ Bioequivalence: Pharmacokinetic and Statistical Considerations. Bethesda MD.

19. Lin, D and WR Fairweather (1991). Experimental design assumptions for alternative stability studies. Paper presented and the annual meeting of the Pharmaceutical Manufacturers Association Biostatistics Subsection. Alexandria VA.

20. Dubey, SD and WR Fairweather (1991). The FDA and its structure. Paper presented at Pharmaceutical Manufacturer's Association Education and Research Institute course in Non-Clinical Statistics, Washington DC.

21. Fairweather, WR (1989). Computer assisted review of tumorigenicity studies. Paper presented at 25th Annual Drug Information Association meeting. Boston MA.

22. _____ (1989). Statistical issues in the evaluation of biological growth factors. Paper presented at 25th Annual Drug Information Association meeting. Boston MA.

23. _____ (1988). Computer-Assisted NDA Review of toxicology and pharmacology data. Paper presented at Joint PMA/FDA-sponsored meeting on CANDAR. Baltimore MD.

24. _____ (1988). Statistical considerations in tumorigenicity study review. Paper presented at 24th Annual Drug Information Association meeting. Toronto, Canada.

25. _____ (1987). Analysis of multiple tumors in carcinogenicity studies. Paper presented at Tenth Annual Midwest Biopharmaceutics Workshop, Muncie IN.

26. _____ (1987). The future of statistics. Paper presented at Tenth Annual Midwest Biopharmaceutics Workshop, Muncie IN.

27. _____ (1987). Estimating changes in bioavailability due to generic substitution of drugs. Paper presented at the annual meeting of the American Statistical Association, San Francisce CA.

28. _____ (1986). Statistical considerations for data format and analysis: An FDA perspective. Paper presented at the Drug Information Association meeting on Organization of Nonclinical Data for Effective Evaluation, Bethesda MD.

29. _____ and Rastogi SC (1986). General considerations for the review of animal tumorigenicity studies. Paper presented at the annual meeting of the Biostatistics Subsection of the Pharmaceutical Manufacturers Association, Washington, DC.

30. _____ (l985). Current issues in the interpretation of animal tumorigenicity studies. Invited paper (welcoming address) presented at the Symposium on Long-term Animal Carcinogenicity Studies--A Statistical Perspective, Bethesda MD.

31. _____ (l985). Multiple comparisons in retrospective studies. Paper presented at the Spring Regional Meetings, Biometric Society, Raleigh NC.

32. _____ (1985). Comparing proportion exposed in case-control studies using several control groups. Paper presented at the International Conference on Foundations of Statistical Inference, Tel Aviv, Israel.

33. _____ and Harris ND (l985). Performance of Peto's test statistics in simulated tumorigenicity studies. Paper presented at the national meeting of the American Statistical Association, Las Vegas, NV.

34. _____ (l984). FDA perspectives in process validation. Invited paper presented at the national meeting of the American Statistical Association, Philadelphia PA.

35. Krushat, WM, SA Edlavitch, GV Quinnan, Jr., E Barker, WR Fairweather, T Hayes, F Rosa, and DB Burlington (l983). Conditional logistic analysis of the reported association between salicylates and Reye Syndrome. Paper presented (by WM Krushat) to Society for Epidemiological Research, Winnipeg, Canada.

36. Fairweather, WR (l982). Quality control and statistics at FDA. Paper presented at meeting of the Quality Control Section of Pharmaceutical Manufacturers Association, Arlington, VA

37. _____ (1982). A model of antibiotic prescribing practices of US physicians: Treatment of URT infections. Paper presented at meeting of the Israel Statistical Association, Jerusalem, Israel.

38. _____ (l982). Statistical aspects of in-vivo/in-vitro correlation. Invited paper presented at 15th Annual Industrial Pharmacy Management Conference, Madison WI.

39. _____ (l978). Some exact, one-sided contingency table tests. Paper presented at the national meeting of the American Statistical Association, San Diego, CA.

40. _____ (l976). Growth curves and bioequivalence--an empirical investigation. Paper presented at the Ninth International Biometric Conference, Boston, MA.

41. _____ (l974). Comments on papers by Metzler and Lyon. Paper presented at the Gordon Research Conference, NH.